REMARKS/ARGUMENTS

Claims 7-29, 33-38, 43, 55, 56, 59-63, 67, 70-87, 92-95 and 117-129 are currently under consideration. Applicants note with appreciation that claims 67 and 126-129 have been allowed. As requested by the Examiner in a telephonic interview on October 21, 2004, Applicants hereby cancel the previously withdrawn claims 39-42, 44-54, 57-58, 64-65 and 96-116. For the remaining claims under consideration, Applicants respectfully request reconsideration in view of the following remarks and claim amendments. Issues raised in the Office Action will be addressed below in the order they appear in the Action.

1. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants traverse this rejection. Claim 38 is drawn to the compositions of claims 22-29, wherein the antigen-binding domain is cross-linked to a polymer. Applicants submit that, contrary to the statement in the Action, the specification provides examples of how to achieve this without destroying the binding activity of the antigen binding domain. For example, in Example 8 of the specification, two anti-HLA-DR antibody fragments, each of which has its V_H chain fused to a FLAG epitope, were cross-linked to each other via an anti-FLAG antibody. This was accomplished by incubating the anti-HLA-DR antibody fragments together with anti-FLAG M2 monoclonal antibody (see page 58 of the specification). In making the rejection, the Examiner simply repeated the reasoning from the last Office Action without specifically addressing Applicants' argument raised in the response dated January 26, 2004. Nevertheless, solely to expedite prosecution of the remaining claims, Applicants hereby cancel claim 38, and reserve the right to pursue claims of similar scope in a future application.

2. Claims 13-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner questioned whether cell lines KARPAS-422, GRANTA-519, LG2 and PRIESS are publicly available (page 3 of the Office Action). Applicants submit

that cell lines KARPAS-422, GRANTA-519, and PRIESS are available through public depositories such as ECACC (European Collection of Cell Cultures) and DSMZ (Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, *i.e.*, German Collection of Microorganisms and Cell Cultures, Ltd). In the response dated January 25, 2004, Applicants already amended claims 13-16 to include their corresponding catalogue numbers. Any one who wishes to use these cell lines can readily obtain them from the public depositories using the catalogue numbers provided. As further evidence of the public availability of cell lines KARPAS-422, GRANTA-519, and PRIESS, Applicants hereby attach printouts from ECACC and DSMZ web catalogues listing these cell lines. The issue regarding LG2, the fourth cell line, is rendered moot by Applicants' amendments of claims 13-16 to delete the recitation of LG2 cell line. Applicants note with appreciation that, in the telephonic interview with the Examiner on October 21, 2004, the Examiner agreed that the evidence of the public availability of the cell lines would be sufficient to overcome the rejection. Accordingly, withdrawal of the rejections are respectfully requested.

3. Claims 7-19, 22-29, 33-38, 43, 55, 56, 59-63, 73-77, 80-87, 92-95, 117-118, 122, 124 and 125 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with written description requirement and enablement requirement. Applicants traverse the rejection and submit that these claims satisfy written description and enablement requirement. Nevertheless, solely to expedite prosecution, Applicants hereby amend claims 17, 18, 20, 22-24, 26, 28, 71, 73-78, 81, 82, 84, 86, 92, 120, 121 and cancel claims 70, 80 and 119 to obviate the rejections.

In addition, Applicants amend claims 22-24, 26, 28 and 126 to delete the recitation of "in a manner where neither cytotoxic entities nor immunological mechanisms are needed for said killing." In a telephonic interview with the Examiner conducted on October 24, 2004, Applicants proposed these amendments and the Examiner indicated that the amendments would be acceptable and would be sufficient to overcome the rejection. Accordingly, withdrawal of the rejections are respectfully requested.

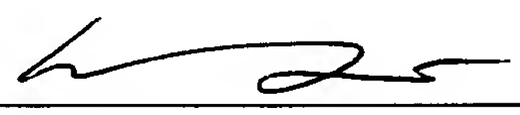
4. Applicants note with appreciation that the Examiner deemed claims 20, 21, 70-72, 78, 79, 119-121 and 123 allowable if rewritten to include all of the limitations of the base claims and all intervening claims. Applicants submit that the base claims, as amended, are now allowable.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner is invited to contact the undersigned at 617-951-7000. A petition for an one-month extension of time, with authorization to charge the required fee to Deposit Account No. 18-1945, Order No. GPCG-P01-003, is being filed concurrently. If a further extension is required, Applicants' attorney respectfully requests that such extension be granted and any fee required be charged to Deposit Account No. 18-1945, Order No. GPCG-P01-003.

Respectfully Submitted,

Date: November 12, 2004



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BACK

HLA Defined

ECACC No. **86052111**
Cell Line Name **PRIESS**

HLA General Parameters

IHW Number	9301
Sex	F
Ethnic Origin	Danish
Consanguineous	No
Homozygous	Yes
WS Region	DEN
Lab Code	SVE
DNA Available from Stock	No
Keywords	Danish 9301

Serological Profile (Class 1 and Class 2 Antigens)

HLA A	2
HLA C	3
HLA B	62
bw4/bw6	6
HLA DP	3 4
HLA DQ	8
HLA DR	4
HLA DR53	53
HLA Dw	4
HLA DPA1*	103
HLA DPB1*	0301 0401
HLA DQA1*	3
HLA DRB4*	101

The ECACC collections represent deposits of cell cultures from world-wide sources. While every effort is made to ensure details distributed by ECACC are accurate, ECACC cannot be held responsible for any inaccuracies in the data supplied. References where quoted are mainly attributed to the establishment of the cell culture and not for any specific property of the cell line, therefore further references should be obtained regarding cell culture characteristics. Passage numbers where given act only as a guide and ECACC does not guarantee the passage number stated will be the passage number received by the customer.

Delivery State

Price Code - A

- (•) Frozen - ?150.00
- ( ) Growing - ?200.00
- ( ) DNA - Please call +44 (0)1980 612512 for Prices.

Quantity Required 1

Prices & Ordering

Click the 'UPDATE' button to refresh the price for the quantity of packs required.
Click the Basket button to add this product to your order.

ecacc European Collection of Cell Cultures

BACK UPDATE

Net Total **?150.00**

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GRANTA-519

DSMZ

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Cell line	GRANTA-519
Cell type	human B cell lymphoma
DSMZ No	ACC 342
Origin	established from the peripheral blood taken in 1991 at relapse o grade B-NHL (leukemic transformation of mantle cell lymphoma, st IV) diagnosed in a 58-year-old Caucasian woman with previous his cervical carcinoma
Depositor	Dr. D. Jayadel, Institute of Cancer Research, Sutton, Surrey, UK
Reference	Rudolph et al., Cancer Genet Cytogenet, 153: 2004, 144-150, PubM
Reference	Jadayel et al., Leukemia, 11: 1997, 64, PubMed ID 9001420
Reference	review: Drexler et al., Leuk Res, 26: 2002, 781, PubMed ID 12127

DSMZ Cell Culture Data

Morphology	spheroid cells growing in suspension, singly or in clumps
Medium	90% Dulbecco's MEM (4.5 g/L glucose) + 10% FBS + 2 mM L-glutamin
Subculture	maintain at 0.5-1.5 x 10^6 cells/ml; split ratio of 1:4 every 3 d out at ca. 1.0 x 10^6 cells/ml
Incubation	at 37 °C with 5-10% CO_2
Doubling time	doubling time of about 49 hours
Harvest	maximum density of about 2.6 x 10^6 cells/ml
Storage	frozen with 70% medium, 20% FBS, 10% DMSO at about 5-7 x 10^6 cells/ampoule

DSMZ Scientific Data

Mycoplasma	contamination was eliminated with BM-Cyclin (tiamulin & minocycl negative in DAPI, microbiological culture, RNA hybridization, PC
Immunology	CD3-, CD10-, CD13(+), CD19+, CD20+, CD30(+), CD34-, CD37+, CD79a+, cyCD79a+, CD80+, CD138+, HLA-DR+, sm/cyIgG-, sm/cyIgM+, sm/cykappa-, sm/cylambda+
Fingerprint	multiplex PCR of minisatellite markers revealed a unique DNA pro
Species	confirmed as human with IEF of AST, LDH, MDH
Cytogenetics	human hypodiploid karyotype with 8% polyploidy; 44(39-44)<2n>XX, -17, -18, +mar, add(1)(p22), del(3)(p14p23), i(8p), i(8q), add(9 t(11;14)(q13;q32), add(13)(p12), add(18)(q21); sideline with tw of der(14) and der(9); carries t(11;14) and rearrangement at 9p2 associated with cyclin D1 activation and deletion of p15/p16; ma published karyotype
Viruses	ELISA: reverse transcriptase negative; PCR: EBV+, HBV-, HCV-, HH , HIV-, HTLV-I/II-

DSMZ | Index | Prices | Dept. of Human and Animal Cell Lines

OIPE NOV 15 2004 PATENT & TRADEMARK

KARPAS-422

DSMZ

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Cell line	KARPAS-422
Cell type	human B cell lymphoma
DSMZ No	ACC 32
Origin	established from the pleural effusion of a 73-year-old woman wit non-Hodgkin lymphoma (intraabdominal, diffuse large cell lymphom refractory, terminal) in 1987; carries t(14;18) IGH-BCL2 fusion (breakpoint in major breakpoint region, MBR)
Depositor	Dr. A. Karpas, University of Cambridge, Cambridge, UK
Reference	Dyer et al., Blood, 75: 1990, 709, PubMed ID 2297573

DSMZ Cell Culture Data

Morphology	round to polygonal cells, growing singly or in small clusters in
Medium	80-90% RPMI 1640 + 10-20% FBS
Subculture	cells are difficult to culture! maintain at 0.5-1.0 x 10^6 cells/ every 3-4 days; seed out with 20% FBS at about 1 x 10^6 cells/ml, possibly no cell growth during first week (we suggest to use fir culture plates); upon thawing viability drops to about 50%
Incubation	at 37 °C with 5% CO_2
Doubling time	doubling time of ca. 60-90 hours
Harvest	maximal density at about 2 x 10^6 cells/ml
Storage	frozen with 70% medium, 20% FBS, 10% DMSO at about 3-5 x 10^6 cells/ampoule

DSMZ Scientific Data

Mycoplasma	contamination was eliminated with BM-Cyclin (tiamulin & minocycl then negative in DAPI, microbiological culture, RNA hybridizatio
assays	
Immunology	CD3-, CD10+, CD13-, CD19+, CD20+, CD34-, CD37+, CD79a+, CD80-, CD138+, HLA-DR+, cyIgM-, cyIgG+, cyIgkappa+, cyIglambda-
Fingerprint	multiplex PCR of minisatellite markers revealed a unique DNA pro
Species	confirmed as human with IEF of AST, NP, PEP B
Cytogenetics	human hyperdiploid karyotype with 10% polyploidy; 47(44-48)<2n>X +14, t(2;10)(p23;q22), t(4;11)(q21;q24), t(4;16)(q21;p13), der(14)t(14;18)(q32;q21)x2
Viruses	ELISA: reverse transcriptase negative; PCR: EBV-, HBV-, HCV-, HH HIV-, HTLV-I/II-